REMARKS

Claims 23-25, 28-41 and 44-58 are pending in this applications. Claims 23, 25, 37, 39, 41 and 48-57 have been withdrawn and are hereby cancelled without prejudice and for reasons unrelated to patentability. Applicant reserves the right to prosecute these claims in another application.

Claims 24, 28 to 36, 38, 40, 44 to 47 and 58 are the subject of the following rejections. Applicant respectfully requests reconsideration of each rejection as follows.

The Office Action of July 11, 2003 rejected claims 24, and 28 to 35 under 35 U.S.C. § 102(b) as being anticipated by Limtrakul. Applicant respectfully requests reconsideration of this rejection as discussed below.

The Office Action responded to applicants' submission of June 23, 2003 that "[n]owhere in Limtrakul do they say that the STI in the soybean milk [that was administered to mice orally] was inactivated. Thus, the same composition as applicants was given to the mice in Limtrakul. Thus, the reference clearly teaches administration of the composition to a mammalian cell." [Office Action of July 15, 2003, p. 2]

Aplicants respectfully submit that the conclusion reached by the Office Action does not appear to be supported in fact in light of the knowledge that soybean trypsin inhibitor has severe gastrointestinal repercussions in mammals who ingest it. Animals **cannot** digest soybean milk with soybean trypsin inhibitor. (See Martin Declaration, ¶ 5, submitted with the March 7, 2002 response) Orally-administered soy products **must** have STI inactivated. (Martin Declaration, ¶ 6) Limtrakul studied 28 mice who were **fed** a diet soybean protein isolate with or, in a separate

group, without soybean milk protein (Limtrakul p. 1591-1592). Nowhere does Limtrakul note that these mice had diarrhea or other symptoms associated with the ingestion of STI. Because the mice were able to eat this diet, the STI must have been deactivated. Therefore, Limtrakul does not teach or suggest the compositions or methods of the pending presented claims. Applicant respectfully asserts that this rejection has been overcome.

The Office Action of July 15, 2003 again rejected claims 24, 28 to 36, 38, 40, 44 to 47 and 58 under 35 U.S.C. § 102(b) as being anticipated by Kosaka. Applicant respectfully requests reconsideration of this rejection on the following basis.

Kosaka teaches the use of papain, which is a cystein protease, not a serine protease. See Vernet T, et al., Structural and Functional Roles of Asparagine 175 in the Cysteine Protease Papain, J. Biol. Chem. 270: 28, 16645-52, July 14, 1995, and Schirmeister T, New Peptidic Cysteine Protease Inhibitors Derived from the Electrophilic Alpha-amino Acid Aziridine-2,3-dicarboxylic acid, J. Med. Chem., 42: 4, 560-72, Feb. 25, 1999 (copies attached to the October 8, 2002 response).

Kosaka teaches the use of papain and citric acid. Applicant claims the use of "soybean milk containing soybean trypsin inhibitor" (as is noted by the Examiner). Papain, which is required by Kosaka, is not soybean milk nor a soybean trypsin inhibitor. Citric acid, required in Kosaka, is not a limitation of Applicant's claims. The mere reference to a particular enzyme *per se* is not a predictor of the behavior of **all** enzymes.

Even when Kosaka mentions that "food and beverage of the present invention can be in a wide variety of forms, such as . . . soybean milk," (Col. 2, lines 43-47) the soybean milk does not contain soybean trypsin inhibitor, as claimed by Applicant. Soybean milk, which is a beverage,

cannot have STI because animals cannot digest STI, and will suffer gastrointestinal problems, if STI is present.

Therefore, Applicants respectfully request reconsideration of this rejection. Furthermore, applicants have respectfully submitted additional claims which relate to the methods of their invention utilizing compositions consisting essentially of soybean milk. As Kosaka does not anticipate applicants' original claims, it certainly does not anticipate applicants' newly presented claims.

The Examiner rejected claims 24, 28 to 36, 38, 40, 44 to 47 and 58 under 35 U.S.C. § 102(b) as being anticipated by Katsumi. Applicant respectfully requests reconsideration of this rejection for at least the following reasons.

Applicants respectfully submit herewith the Declaration of Dr. Robert Zivin in explanation of the distinction between active STI and denatured STI. When a protein such as STI is subjected to heat, as is necessary in order to obtain ingestible soybean milk, the protein is said to be "denatured". As set forth in the Zivin Declaration, "proteins are defined by both (1) their chemical structure, which includes its substituent amino acids as wellas their unique conformation and (2) their biological function." [Zivin Declaration, ¶1]. The protein's particular conformation is characteristic of each specific protein type, thus the "conformation is an important aspect of protein structure and identification." [Zivin Declaration, ¶3].

Protein denaturation, as set forth in the Zivin Declaration, is "the process of altering the native/low free energy conformation of a protein" [Zivin Declaration, ¶4]. This causes an opening of the protein's conformation, which eliminates the protein's biological activity and often causes the protein to precipitate out of solution, thus removing it from the composition in

which it resides. [Zivin Declaration, ¶5]. Thus, in the case of the soybean trypsin inhibitor protein, upon exposure to heat, the protein is no longer active as a trypsin inhibitor because (1) the protein is denatured and therefore no longer the same protein; and/or (2) the protein may, in fact, have precipitated out of solution and may no longer be present in the composition. Even if the constituent molecules present in the protein are present in a composition, however, these constituents no longer have biological activity and cannot be said to be "present" in the form of the original protein in the composition.

Applicants respectfully submit that Katsumi teaches the use of soybean milk, which was originally used for consumption, as a topical application. Soybean milk (as used in Katsumi) can be treated with salt and heat to yield "cheese-like tofu," and such soybean milk was consumed prior to Katsumi, who recognized its use topically. See Katsumi, page 2. However, soybean milk that has been processed for consumption such as that in Katsumi, has the STI and BBI activity eliminated, since these proteins inhibit digestion and result in diarrhea (see Declaration of Katharine Martin, paragraph 4 and 6). The compositions of applicants' invention require that STI and BBI activity be retained, active and non-denatured (see Declaration of Katharine Martin, paragraph 3), which would prevent the consumption of these composition. The Katsumi reference does not have the same composition applied in the same way as that claimed, as is readily apparent in this response. Therefore, Applicant respectfully requests reconsideration of this rejection.

The Office Action of July 15, 2003 has provisionally rejected claims 24, 28-36, 38, 40, 44-47 and 58 under 35 USC § 102(e) as being anticipated by copending Application No. 09/110,409. Inventor Miri Seiberg was the inventor for both the claimed invention in the

relevant claims and the invention disclosed, but not claimed in the 09/110,409 application, and is therefore not the invention "by another."

The Office Action of July 15, 2003 has rejected claims 24, 28-36, 38, 40, 44-47 and 58 under 35 USC § 103 as being unpatentable over Limtrakul taken with Kosaka or Katsumi. Applicant reasserts its arguments above and respectfully requests reconsideration of this rejection for at least the foregoing and following reasons.

Limtrakul does not teach the use of "soybean milk containing soybean trypsin inhibitor." The composition used by Limtrakul is used in a dietary manner, whereas Applicant's claimed "soybean milk containing soybean trypsin inhibitor," would not be digestable by animals, including humans. Further, many of Applicant's claims require topical application of the composition, and Limtrakul does not apply soybean milk with STI topically.

Neither Kosaka nor Katsumi teach the use of soybean milk with STI. Kosaka uses a cystein protease, and citric acid, but not soybean milk with STI. Katsumi teaches a topical use of nutritional soybean milk, which is distinctly different from soybean milk with STI, which is not digestible and causes gastrointestinal problems upon ingestion.

Neither combination of Limtrakul and Kosaka or Katsumi meets all of the limitations of Applicant's claims and therefore, Applicant believes that this rejection is overcome.

The Office Action of July 15, 2003 provisionally rejected claims 24, 28-36, 38, 40, 44-47 and 58 over claims 1-60 of Application No. 09/110,409 on the basis of obviousness-type double patenting. Applicant notes that Application No. 09/110,409 has not yet issued as a patent. In the event the patent does issue, Applicant will file an appropriate terminal disclaimer.

CONCLUSION

Applicant respectfully asserts that the application is in condition for allowance. Reconsideration and the early issuance of a Notice of Allowance are requested. If the Examiner has any outstanding issues, the courtesy of a telephone call is requested.

Authorization of Deposit Account

The Commissioner is hereby authorized to charge any fees or credit any overpayment, to Deposit Account 10-0750/JBP438/ALC. Three copies of this page are enclosed. This authorization also hereby includes a request for any extensions of time of the appropriate length required upon the filing of any reply during the entire prosecution of this application.

Respectfully submitted,

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